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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,671	10/28/2003	Robert D. Ivarie	021396-000203US	6850
20350	7590	09/19/2008	EXAMINER	
TOWNSEND AND TOWNSEND AND CREW, LLP			KAUSHAL, SUMESH	
TWO EMBARCADERO CENTER				
EIGHTH FLOOR			ART UNIT	PAPER NUMBER
SAN FRANCISCO, CA 94111-3834			1633	
			MAIL DATE	DELIVERY MODE
			09/19/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/696,671	IVARIE ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Sumesh Kaushal	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 13 June 2008.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 20, 31, 33-34, 37, 41, 46, 52-57, 62-98 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_ is/are allowed.
- 6) Claim(s) 20,31,33,34,37,41,46,52-57 and 62-98 is/are rejected.
- 7) Claim(s) \_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____ .                                     |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date ____ .   | 6) <input type="checkbox"/> Other: ____ .                         |

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## **DETAILED ACTION**

Applicant's response filed on 06/13/08 and 03/06/08 has been acknowledged and fully considered.

*Claims 20, 31, 33-34, 37, 41, 46, 52-57, 62-98 are pending and are examined in this office action.*

*The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.*

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/14/08 has been entered.

The restriction requirement mailed on 05/29/08 has been withdrawn in view of telephonic interview conducted on 06/25/08.

### ***Claim Rejections - 35 USC § 112***

Claims 20, 31, 33-34, 37, 41, 46, 52-57, 62-98 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a germ-line transgenic chicken which lays an egg containing an exogenous protein encoded by a transgene selected from group consisting of NLB-CMV-IFN $\alpha$ 2, NLB-CMV-EPO and NLB-CMV-G-CSF present in the germ-line of the transgenic chicken wherein the exogenous protein is produced in the transgenic chicken's oviduct and is deposited in the egg-while of the eggs produced, does not reasonably provide enablement for any other germline transgenic chicken that lays eggs containing any exogenous protein

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encoded by a transgene present in the germline of the transgenic avian. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

#### **Response to Argument (enablement)**

The applicant has amended the instant claims to recite transgenic chicken whose genome contains a transgene introduced by a retroviral vector, wherein the oviduct cells produces and secrete the exogenous protein into oviduct lumen. However the scope of transgenic chicken (as claimed) encompasses a transgenic chicken which lay eggs containing any exogenous protein of interest (see claim 124). This would require an excessive and undue amount of experimentation because the retroviral-based vectors are not tissue specific and are known to integrate in the host genome in a random fashion. Therefore making and screening chickens that produce any exogenous protein (*i.e. interferon (IFN), erythropoietin (EPO), human growth hormone, lysozyme, and beta-casein, albumin, alpha-1 antitrypsin, antithrombin III, collagen, factors VIII, IX, X, fibrinogen, hyaluronic acid, insulin, lactoferrin, protein C, granulocyte colony-stimulating factor (G-CSF), granulocyte macrophage colony-stimulating factor (GM-CSF), tissue-type plasminogen activator (tPA), somatotropin chymotrypsin, antibodies and immunotoxins etc*) would require excessive and undue amount of experimentation (to screen for transgenic chickens that have the asserted transgenic phenotype) which is not considered routine in the art of avian transgenic.

At best the specification as filed discloses the making of chimeric chickens by transducing stage X embryos with NLB-CMV-BL (ALV-based vector) transduction particles (spec page 32, example-3, page 33 lines 3-9) but falls short of disclosing any transgenic bird. At very best the Dr. Ivarie's declaration discloses transgenic chickens which are capable of producing the IFN $\alpha$ 2, EPO and G-CSF in the egg-white, using NLB-CMV-based vector system which randomly integrated in the oviduct cells that produces egg-white.

It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). In the

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instant case the state of the art at the time of filing regarding making germ-line transgenic birds that produces an exogenous protein of interest in the eggs is considered highly unpredictable especially in view of low transgene transmission to the progeny. The integration of viral vectors especially retroviral vectors like ALV in the genome is random which renders any tissue specific expression (i.e. oviduct) highly unpredictable even in the presence of tissue specific promoter. Therefore it would require an undue and excessive amount of experimentation to make a chicken that produces egg containing any exogenous protein of interest. The lack of understanding of essential genetic control elements make it difficult to predict the behavior of a transgene in any and all avian because the expression is influenced by position effect in transgenic animals. The individual gene of interest, promoter, enhancer, coding or non-coding sequences present in the transgene construct and the site of integration, for example are the important factors that govern the expression of a transgene. Therefore the phenotype of transgenic animal is greatly dependent upon the expression vector used and the presence of tissue specific control elements therein.

For example, invention as claimed reads upon a transgenic chicken that produces *immunotoxins*. Making such a transgenic chicken is considered highly unpredictable due to the deleterious effect of immunotoxin produced not only in oviduct but also in the blood stream of the transgenic animal, which would not render the animal to transmit its genes to its progeny. Similarly the scope of invention as claimed is not restricted to localize expression (i.e. using oviduct specific promoters) of gene of interest, which would result in systemic expression of the transgene product with unpredictable consequences. For example, a transgene expression any antibody in systemic circulation would result in humoral abnormalities (i.e. cytolysis, inflammation, agglutination etc.) severely affecting the animal's survival and its ability to produce transgenic progeny. The state of the avian transgenic remains unpredictable, since there are many hurdles to over come (see Sang Mechanisms of Development 121:1179-1186, 2004, Mozdziak et al, Developmental Dynamics 229:414-421, 2004 ref of record). Therefore considering the scope of invention especially in view of the state of the art, one skill in the art would have to engage in excessive and undue amount of

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experimentation to practice the invention as claimed. For example, it would require an extensive and undue amount of experimentation to screen chimeric birds and progeny thereof that would produce any protein of interest in transgenic eggs via oviduct expression.

At issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See *Fields v. Conover*, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). In instant case making a germ line transgenic chicken capable of producing eggs that contains any exogenous protein of interest by extensive screening of chimeric birds and progeny thereof is not considered routine in the art and without sufficient evidence that any transgene construct of interest is capable of transmitting to the progeny with oviduct specific expression, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

### ***Double Patenting***

Claims 20, 31, 33-34, 37, 41, 46, 52-57, 62-98 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22 of copending Application No. 11/337,302, for the reason of record as set forth in the office action mailed on 11/14/07.

Claims 20, 31, 33-34, 37, 41, 46, 52-57, 62-98 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 11/274,674, for the reason of record as set forth in the office action mailed on 11/14/07.

Claims 20, 31, 33-34, 37, 41, 46, 52-57, 62-98 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 of copending Application No. 11/100,255, for the reason of record as set forth in the office action mailed on 11/14/07.

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Claims 20, 31, 33-34, 37, 41, 46, 52-57, 62-98 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 of copending Application No. 11/099,934, for the reason of record as set forth in the office action mailed on 11/14/07.

Claims 59-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 11/337,361, for the reason of record as set forth in the office action mailed on 05/15/07, for the reason of record as set forth in the office action mailed on 10/30/07.

Claims 20, 31, 33-34, 37, 41, 46, 52-57, 62-98 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-26 of copending Application No. 11/376,023, for the reason of record as set forth in the office action mailed on 10/30/07.

Claims 20, 31, 33-34, 37, 41, 46, 52-57, 62-98 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 124-129, 132-142, 145-153, 156, 158 and 160-164 of copending Application No. 10/463,980.

#### **Response to Argument (double patenting)**

The applicant argues that should any one of the cited co-pending applications issue before the allowance of the present application, applicant is willing to consider the possibility of filing an appropriate terminal disclaimer. Therefore the rejections above has been maintained.

#### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sumesh Kaushal/  
Primary Examiner, Art Unit 1633

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